

<https://helda.helsinki.fi>

---

## Surgery and health-related quality of life-A prospective follow up study on breast cancer patients in Finland

Rautalin, Mervi

2021-07

---

Rautalin , M , Jahkola , T & Roine , R P 2021 , ' Surgery and health-related quality of life-A prospective follow up study on breast cancer patients in Finland ' , European Journal of Surgical Oncology , vol. 47 , no. 7 , pp. 1581-1587 . <https://doi.org/10.1016/j.ejso.2021.02.006>

---

<http://hdl.handle.net/10138/333421>

<https://doi.org/10.1016/j.ejso.2021.02.006>

---

cc\_by

publishedVersion

---

*Downloaded from Helda, University of Helsinki institutional repository.*

*This is an electronic reprint of the original article.*

*This reprint may differ from the original in pagination and typographic detail.*

*Please cite the original version.*



# Surgery and health-related quality of life – A prospective follow up study on breast cancer patients in Finland

Mervi Rautalin <sup>a,\*</sup>, Tiina Jahkola <sup>b</sup>, Risto P. Roine <sup>c</sup>

<sup>a</sup> Department of Plastic Surgery, Helsinki University Hospital and University of Helsinki, Finland

<sup>b</sup> Department of Plastic Surgery, Helsinki University Hospital, Finland

<sup>c</sup> Department of Health and Social Management, University of Eastern, Finland

## ARTICLE INFO

### Article history:

Accepted 3 February 2021

Available online 9 February 2021

### Keywords:

Breast cancer

Breast cancer surgery

Health-related quality of life

Breast reconstruction

Breast cancer surgery outcome

PROM

## ABSTRACT

**Introduction:** The influence of different surgical approaches on breast cancer patients' Health-related Quality of life (HRQoL) is an important determinant when making decisions on the choice of treatment. Knowledge on how patients actually perceive different surgical treatments regarding long-term HRQoL is still scarce.

**Materials & methods:** 1065 patients with primary breast cancer operated on from 2008 to 2015 at Helsinki University Hospital, Finland were prospectively followed-up for two years. They filled in two HRQoL questionnaires, the EORTC QLQ C30 – BR 23 and the 15D, at baseline and at 3, 6, 12 and 24 months after surgery. Clinical data on treatments given and the course of recovery were collected from patient records. Patients were divided into four mutually exclusive groups according to surgical method: breast resection (n = 415), oncoplastic resection (n = 248), mastectomy (n = 351) and immediate reconstruction (n = 51). Clinical data were combined with HRQoL scores and analysed as multivariate modelling.

**Results:** All groups experienced initially worsening overall HRQoL after baseline. Oncoplastic resection patients had the best body image and their HRQoL reached the highest level after treatments at 12 months whereas the reconstruction patients reached the highest HRQoL level first at 24 months. Mastectomy patients had the lowest scores throughout the 24-month follow-up.

**Conclusion:** Extensive surgery, in terms of immediate reconstruction, led to slower HRQoL recovery than oncoplastic techniques. Mastectomy patients are at risk of having the lowest HRQoL scores throughout their recovery after surgery.

© 2021 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

## Introduction

The method and timing of surgical treatment of breast cancer is determined by the stage of the disease, general health of the patient and patient's and surgeon's preferences. Breast cancer operations differ in anatomical extent and treatment related morbidities [1,2]. Studies have indicated that the oncological safety is similar independent of the surgical method [3–5]. Less is known about the effect of the surgical method on Health-related quality of life (HRQoL) which is considered an important aspect of high-quality healthcare [6]. There are a number of different options for

evaluating breast cancer patients perceived well-being, ranging from historical self-assessment with questionnaires to modern validated tools with specific and/or targeted questionnaires [7–9]. Studies on surgical methods reflecting HRQoL are still scarce, often not prospective, and limited in their comparison of surgical methods [3,6]. A recent systematic review addressed breast cancer patients HRQoL and surgical methods based on studies in which breast reconstruction was compared to mastectomy and breast-conserving surgery. The systematic review included 16 eligible studies in its meta-analysis the main findings of which were: breast reconstruction and breast-conserving surgery both produce better HRQoL outcomes in comparison to mastectomy. In addition, the review concluded that it would be beneficial to incorporate both breast/surgery specific and generic HRQoL instruments into breast cancer studies to cover the heterogeneity of study groups [10]. Another recent, retrospective, study compared breast-conserving

\* Corresponding author. Helsinki University Hospital, Department of Plastic Surgery, Töölö Hospital, Topeliuksenkatu 5, 00029, HUS, Helsinki, Finland.

E-mail addresses: [mervi.rautalin@hus.fi](mailto:mervi.rautalin@hus.fi), [mervi.rautalin@helsinki.fi](mailto:mervi.rautalin@helsinki.fi) (M. Rautalin).

surgery to reconstruction using a breast specific HRQOL instrument, the BREAST-Q. The study reported that breast-conserving surgery was associated with less complications and need for revisional surgery in comparison to both allogeneous and autogenous reconstruction methods. Furthermore, breast conserving surgery led to better sexual well-being and satisfaction with the breast [11]. Our study complements the above mentioned studies by investigating breast cancer patients HRQOL in a prospective manner with both breast cancer specific (EORTC QLQ-C30- BR23) and generic (15D) HRQoL instruments. Furthermore, to find out whether different surgical methods lead to different HRQOL results or complications, our study includes all different surgical method groups: breast-conserving surgery, mastectomy and breast reconstructing methods. HRQOL is an important aspect when choosing surgical modalities for breast cancer patients.

## Material and methods

### Patients

1065 patients diagnosed with primary breast cancer at Helsinki and Uusimaa Hospital District (HUS) Finland between September 2008 and September 2015 participated in the study. Participation did not affect the treatment plan or offer financial compensation for the patients. The study was approved by the University of Helsinki Ethics committee (Permission 68 (June 11, 2008, 207/13/03/02/08)). Part of the patients (n = 130) received also peer support in the context of a concomitant randomized substudy in addition to usual care.

### Questionnaires

Patients filled in an informed consent form and two quality of life questionnaires: the generic 15D and the cancer specific EORTC QLQ30-C30 with its QLQ-BR23 breast cancer specific module [8,9]. The questionnaires were collected at the time of diagnosis and later at 3, 6, 12 and 24 months after primary surgery. The generic and the cancer-specific HRQoL instrument complement each other and provide a wider perspective than a disease-specific instrument alone. Both instruments are well established and have been used widely to study breast cancer patients [12–16].

The 15D is a generic HRQoL instrument, which produces an overall quality of life score and a health profile. The questionnaire consists of 15 dimensions (Mobility, Vision, Hearing, Breathing, Sleeping, Eating, Speech, Excretion, Usual Activities, Mental Function, Discomfort and Symptoms, Depression, Distress, Vitality, Sexual activity). Each dimension is rated by the patient from 1 (best situation) to 5 (worst situation). In comparing the 15D scores, the minimum clinically important difference (change) (MID) is 0.015 [17].

The EORTC QLQ-C30 is a cancer-specific HRQoL instrument developed by the European Organisation for Research and Treatment of Cancer. It is validated in more than 100 countries and in wide use around the globe. The EORTC QLQ-C30 produces functional status and symptom scores, which patients rate from 1 to 4 and 1 to 7 accordingly. It also provides an overall Quality of life score. The BR23 is a set of 23 breast cancer specific questions which produce 4 functional scores (Body Image, Sexual functioning, Sexual enjoyment and Future perspective) and 4 symptom scores (Systemic therapy side effects, Breast symptoms, Arm symptoms and Upset by hair loss). Scores range from 0 to 100. For functional scores a high score indicates good health whereas for symptom scores a high score indicates problems in that area [9]. The significance of the changes in the EORTC score can be interpreted as minimal for a score change between 5 and 10, intermediate for a

change between 10 and 20, and large for a change >20 [18]. A MID for the EORTC has not been firmly established and there is some variation in the interpretation of the absolute values within different studies [16,19].

### Clinical data

Hospital records were viewed for medical data on patients' health status, treatments given, and the course of surgical care. Patients were divided into groups depending on the type of primary surgery: resection of the breast (n = 415), oncoplastic resection (n = 248), mastectomy (n = 351), and immediate reconstruction (n = 51).

Resection and oncoplastic resection were identified as being either a simple resection of the breast cancer site with/without skin and underlying fascia removed with moderate reshaping of breast tissue if needed, or oncoplastic resection, which included removal of the tumour and more excessive remodeling, reshaping and/or replacing breast tissue with/without repositioning of the nipple in order to achieve better cosmesis. Unlike the oncoplastic group, the reconstruction group included also use of pedicled flaps. Thus the classification we use for oncoplastic resection differs slightly from some other classifications of oncoplastic methods (level 2 techniques) [4,20]. The codes and techniques of the surgical methods used were recorded from patient records. Based on the Nordic Classification of Surgical Procedures (NCSP), oncoplastic resection is defined by code HAB50 and thus differentiated from resection of the breast HAB40 or lumpectomy HAB99.

The Reconstruction group consisted of patients who underwent immediate breast reconstruction by either implants or autologous tissue reconstruction (or both combined). Autologous tissue reconstruction included both pedicled and microsurgical flaps.

Data on comorbidities were collected from hospital records using the ICD-10 for identifying medical conditions. The Charlson comorbidity index was used with the latest suggested rating for the comorbidities (where certain comorbidities get higher and some lower points compared to the initial introduction of the index) [21–23]. In addition we recorded patients' body-mass index (BMI), smoking status and diabetes status if available, as those are considered important influencers of HRQoL and factors that might correlate with complications [24,25].

Complications were identified as a recorded abnormality in the normal recovery process after surgery. They included wound healing, bleeding and thromboembolic complications leading to need of medication and/or extra procedures. Excessive seroma formation needing aspiration more than 10 times was noted as a potential independent factor influencing HRQoL even though having seroma is considered to be part of the healing process and not an actual complication.

### Statistical analysis

The distribution of results for both HRQoL instruments was slightly skewed. Therefore, non-parametric tests (Kruskal-Wallis) were used in the analyses. For regression analysis we performed a Box-Cox transformation to ensure normality of the data. Statistical analysis was performed using SPSS 25.0 software and partly NCSS software. We performed a stepwise linear regression analysis (One-way ANOVA) to find possible explanatory factors affecting HRQoL. Variables chosen for analysis were: tumour specifics (T-, N-, M-classification, Grade of the disease), BMI, oncological treatments (radiation therapy, chemotherapy and hormonal treatment), whether or not having complications, excessive seroma formation (seroma aspirated more than 10 times), multiple surgery and recurrence of the disease.

## Results

### Patient characteristics

The age of the 1065 patients varied from 24 to 89 (Mean 59.7 years, SD 10.4) reconstruction patients being approximately 10 years younger than patients in the other groups. Part of our study population ( $n = 130$ ) received peer support via telephone. In that randomized intervention study there was no statistically significant difference in participants' overall HRQoL compared to the controls [26]. We also compared those patients overall HRQoL at all timepoints to that of the whole cohort but found no statistically significant difference in the change of HRQoL.

Two breast cancer patients were male, 48 had had an earlier breast cancer and 39 some other cancer at baseline. 107 patients were active smokers.

The Charlson comorbidity points varied from 0 (no significant comorbidities) to 1–7 (Mean 0.327, SD 0.733). Most of the recruited patients ( $n = 844$ ) had no comorbidities. 119 patients had 1 point, 85 had 2 points and 14 had 3 points. Patients with Charlson index  $\geq 4$  ( $n = 3$ ) were excluded because of small group size. 72 patients were diabetics.

### Treatment

351 patients had mastectomy, 415 breast resection, 248 oncoplastic resection and 51 immediate breast reconstruction (of which 76% were autologous). 402 patients had axillary clearance, the rest sentinel node biopsy or no biopsy at all (DCIS with no immediate reconstruction).

Radiation therapy was given to 840 patients (79% of all), 523 (49%) received chemotherapy, and 766 (72%) endocrine treatment. 119 (11%) patients received targeted therapy (anti HER2-medication). Table 1 shows patient characteristics within the treatment groups.

### Follow up

105 (10%) patients had post-surgery wound infection and 32 (3%) some other complication. 18 (13%) of those having a complication were diabetic. 102 (10%) patients needed more than one surgical operation at baseline and 26 (2%) additional surgery after oncological treatments. This was due to positive margins or late

axillary clearance after positive sentinel node biopsy. 309 (29%) patients had post-surgery seroma. Of them 43 (4%) had to have the seroma aspirated more than 10 times. 16 patients (1.5%) died, 32 (3%) patients had a recurrence and 22 (2%) another malignancy during follow-up. 50 patients (14% of mastectomy group) underwent delayed breast reconstruction during the two-year follow-up.

### Response rate and missing data

During our study period of two years, patients who were willing to participate and fill in the questionnaires, did so quite conscientiously. Response rates are listed in Table 1. The number of missing answers was similar in all groups at all timepoints thus not affecting the analysis. Questions concerning sexual wellbeing were most often left unanswered. Some data were missing at baseline from around 5% of all respondents and the amount of missing data increased a bit with time: at 12 months some data were missing from 7.3% to 14.2% and at 24 months from 14.3 to 19.5% of respondents, depending on the question.

### HRQoL results

Age had a statistically significant effect on HRQoL measured with the 15D (tested with Spearman correlation,  $p = 0.008$ ) whereas it did not affect the EORTC results in a statistically significant manner ( $p = 0.396$ ).

Comorbidities affected HRQoL negatively when measured with the 15D ( $p < 0.000$ ) but not when measured with EORTC ( $p = 0.071$ ). BMI correlated negatively with HRQoL with both instruments and at all measuring points ( $p < 0.05$ ).

Active smoking ( $p = 0.023$ ) and higher BMI ( $p = 0.006$ ) correlated statistically significantly with the occurrence of complications, whereas diabetes ( $p = 0.561$ ) did not.

Patients who had to go through more than 10 times of seroma aspiration, experienced some negative effect on HRQoL at 6 months measured with the 15D ( $p = 0.040$ ). Having to go through more than one surgical procedure, irrespective of the reason, did not seem to affect HRQoL with either measuring tool. Axillary clearance correlated negatively with HRQoL based on both instruments from 3 months to 12 months ( $p < 0.01$ ) but only EORTC showed negative correlation on HRQoL in axillary clearance patients still at 24 months ( $p = 0.002$ ).

The higher the tumour grade, the poorer the HRQoL measured

**Table 1**  
Patient characteristics. DCIS = ductal carcinoma in situ.

	Resection $n = 415$	Oncoplastic Resection $n = 248$	Mastectomy $n = 351$	Reconstruction $n = 51$
<b>Age mean (SD)</b>	61.7 years (8.6)	59.4 years (8.6)	59.1 years (12.1)	48.5 years (11)
<b>Axillary clearance n (%)</b>	86 (21)	87 (35)	210 (60)	19 (37)
<b>Oncological treatment</b>				
<b>Radiation therapy n (%)</b>	413 (100)	239 (96)	171 (49)	17 (33)
<b>Chemotherapy n (%)</b>	131 (32)	129 (52)	231 (66)	32 (63)
<b>Endocrine treatment n (%)</b>	279 (67)	187 (75)	266 (76)	34 (67)
<b>Tumour characteristics</b>				
<b>Ductal carcinoma n (%)</b>	296 (71)	167 (67)	218 (62)	27 (53)
<b>Lobular carcinoma n (%)</b>	58 (14)	41 (17)	96 (27)	13 (26)
<b>DCIS n (%)</b>	18 (4)	7 (2.8)	11 (3)	5 (10)
<b>T1/T2/T3/T4 n (%)</b>	348(84)/60(15)/1(0)/0	170(69)/75(30)/2(1)/0	152(43)/159(45)/28(8)/8(2)	31(61)/16(3)/3(6)/0
<b>N0/N1/N2/N3 n (%)</b>	317(76)/83(20)/12(3)/3(1)	150(61)/73(29)/20(8)/5(2)	154(44)/122(35)/54(15)/20(6)	32(63)/16(31)/3(6)/0
<b>Grade 1/2/3 n (%)</b>	170(41)/151(36)/92(22)	69(28)/105(42)/74(30)	62(18)/131(37)/157(45)	5(10)/20(39)/25(49)
<b>15D/EORTC Response %</b>				
<b>3 Months</b>	96.1/95.7	93.9/92.3	93.9/92.5	94.1/92.2
<b>6 Months</b>	96.9/95.4	95.1/92.7	97.1/94.8	98/96.1
<b>12 Months</b>	95.2/95.2	94.7/93.1	96/93.9	98/96.1
<b>24 Months</b>	90.6/89.6	88.6/86.5	91.5/90	92.2/90.2

with both instruments at 3 months. By contrast, larger tumour size (T-classification) affected only HRQoL measured with the EORTC at 12 months. Nodal status (N-classification) was significantly negatively associated with HRQoL at all measuring points with the 15D but with the EORTC only at 3 months. Distant metastasis (M-classification) influenced HRQoL measured with the EORTC at 24 months. Detecting a recurrence did not impair HRQoL. Of the oncological treatments, radiation therapy or hormonal treatment did not affect HRQoL, but chemotherapy led to deteriorated HRQoL especially at 6 months. Table 2 represents regression analyses results.

Appendix 1 shows the mean 15D scores at different timepoints for different groups. In all groups the mean score deteriorated in a clinically important manner from baseline to 3 months. Of the treatment groups, the oncoplastic resection group showed clinically important improvement from the initially worst situation (at 3 months) at 12 and 24 months, and the reconstruction group at 24 months. In the resection and mastectomy groups the 15D score did not improve in a clinically significant manner from the 3-month lowest level during the entire 24-month follow-up.

Based on both instruments, the mastectomy group had the lowest HRQoL score at baseline and at 24 months compared to the other groups. According to the EORTC, the reconstruction group had the most marked improvement of HRQoL at 24 months. Fig. 1 and Fig. 2 show mean HRQoL scores within groups by time.

The EORTC symptom scales showed constantly that fatigue, pain and sleeping were impaired in all groups at all measuring points.

The mastectomy group reported pain more than the other groups throughout the study, but the differences were statistically significant only at baseline.

To study the difference of EORTC patient-reported symptoms between our study groups we did a variance analysis for all the studied time points with all reported symptom scales. Tables 3 and 4 demonstrate those EORTC results that were different between study groups at timepoints baseline and 24 months.

Based on EORTC Functional scales, reconstruction patients had the best Physical and Sexual functioning throughout the study compared to the other groups. Their social functioning scale was the best at baseline and at 24 months, but their Body image score was the worst of all groups at 24 months. When comparing changes in mean EORTC scores at 24 months, there were statistically significant differences between groups in Financial difficulties, Physical functioning, Body image, Sexual functioning and Arm symptoms. Body image also decreased in a clinically significant manner (intermediate 10–20-point change) from baseline to 24 months in the mastectomy and reconstruction groups. In arm symptoms, the oncoplastic and mastectomy groups reported a

minimally clinically important decrease (5–10 points) in EORTC points [18]. At 12 months, patients who had delayed reconstruction did not differ from the rest of the mastectomy patients. At 24 months, there was only a small and insignificant difference in the EORTC global score (74.32 in the mastectomy group compared to 73.84 with delayed reconstruction). However, regarding the 15D, the delayed reconstruction patients reported a borderline clinically importantly better total 15D score at 24 months compared to the rest of the mastectomy patients (0.915 vs 0.890).

## Discussion

Our prospective study describes the healing process of breast cancer patients in Finland's biggest breast cancer and plastic surgery units. We used well established and accepted HRQoL questionnaires available at the time of onset of this study. Unfortunately, data on baseline response rate is missing as the recruitment process was long and interrupted at some time points to allow collection of data for some other breast cancer projects of the hospital. As a consequence of that, we are not absolutely certain about the baseline response rate and do not report it here. However, once the patients had agreed to participate, they responded to the follow-up questionnaires very well as evidence by the high response rates over 90%.

The amount of missing data was similar in all groups. Questions about sexual wellbeing seemed to be the most difficult to answer for all patients. Searching for common factors for non-response did not reveal any obvious reasons; some patients did not answer at some timepoints but then answered at the next one whereas some patients suffering from recurrence returned all questionnaires at all timepoints. Neither the mean age nor the number of complications differed between respondents and non-respondents. The only difference we found was in the mastectomy group in which the group of non-respondents comprised a larger percentage of patients having received chemotherapy (76% vs. 66%). However, we have no reason to assume that some groups would be over- or underrepresented in our study.

High research activity and multiple ongoing studies in our clinic affected the quite long recruitment period of our study: at times we were forced to halt our recruitment process so that the burden caused by studies for the same patients didn't get too high.

At the onset of our study, in year 2008, the proportion of oncoplastic techniques of all breast conserving techniques was 13.8%. That proportion had risen to 44.3% in year 2011, and thereafter varied yearly from 31.9% to 48.3%. All study patients received similar oncological treatment regardless of when they were recruited to the study. In Finland, reconstruction methods have

**Table 2**

Regression analysis results. Statistical significance (p-values) and standard coefficients of nominated factors' effect on overall HRQoL at measuring points: EORTC above, 15D below in box.

Variable		3 Months		6 Months		12 Months		24 Months	
		p-value	Std Co	p-value	Std Co	p-value	Std Co	p-value	Std Co
Grade	EORTC	0.015*	-0.094	ns		ns		ns	
	15D	0.000***	-0.150	ns		ns		ns	
T - class	EORTC	ns		ns		0.014*	-0.086	ns	
	15D	ns		ns		ns		ns	
N - class	EORTC	0.000***	-0.174	ns		ns		ns	
	15D	0.001***	-0.131	0.032*	-0.079	0.001***	-0.106	0.002**	-0.103
M - class	EORTC	ns		ns		ns		0.032*	-0.071
	15D	ns		ns		ns		ns	
BMI	EORTC	0.012*	-0.094	-		-		-	
	15D	0.002**	-0.113						
Chemotherapy	EORTC	-		0.000***	-0.245	0.032*	-0.075	0.013*	-0.082
	15D	-		0.000***	-0.158	ns		ns	

\*p < 0.05, \*\*p < 0.01, \*\*\*p < 0.001.



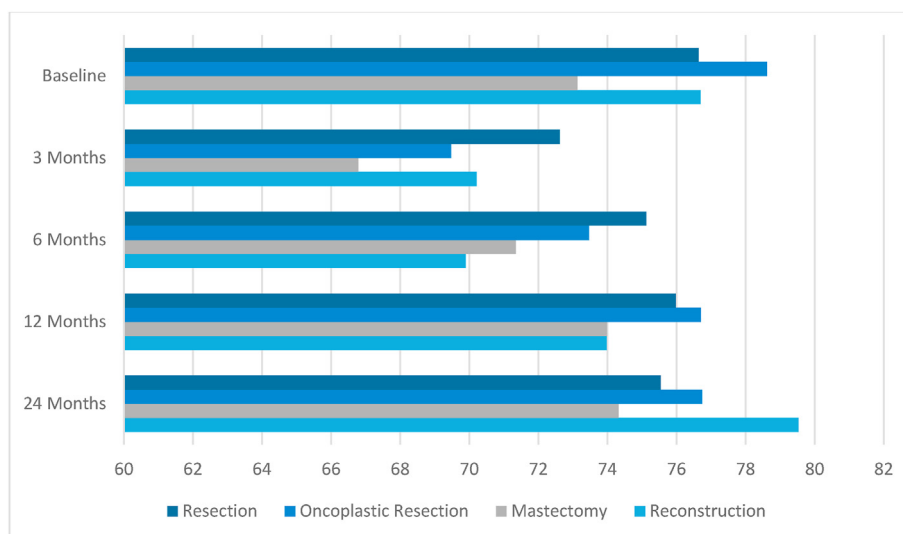


Fig. 1. Mean EORTC HRQoL scores for the study groups by time.

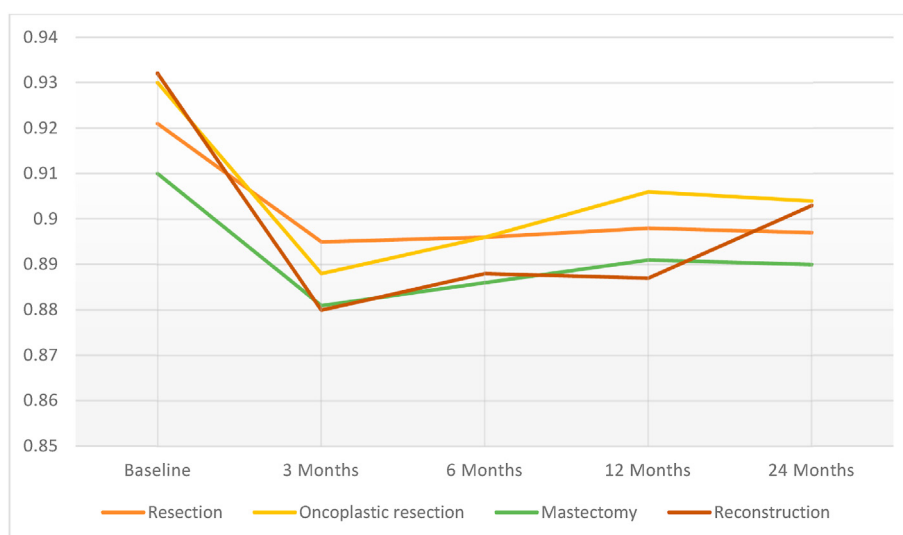


Fig. 2. Mean 15D HRQoL scores for the study groups by time.

traditionally been more autologous than implant-based and this has not changed radically over time. This may be a cultural difference as our clinic has a strong tradition of microsurgical reconstruction - or a result of our easily accessible and virtually free health care for the patient. Patients pay for their hospital stay, but the extent of the surgical procedure is not a financial issue for the patient – the amount of personal cost being the same whether they have a resection procedure or a microsurgical operation.

Both EORTC and 15D describe the healing process of breast cancer patients well. The ceiling effect (patients reporting perfect health) was relatively low at baseline for both instruments: 8% for 15D and 15.3% for EORTC. At later measurement points the ceiling effect was even lower. Mastectomy patients had the lowest reported HRQoL at baseline and at 24 months, which might be because of a heavier disease burden. According to generally approved guidelines regarding which patients can be offered immediate reconstruction, the reconstruction group is probably healthier in many aspects. Still, all breast cancer patients deserve careful planning on what would be the best surgical approach for each individual [25].

Methods of breast reconstruction cannot be randomized because surgical treatment is always tailored for each patient. Following the AMAROS-study, the international guidelines for breast cancer treatment have changed and nowadays axillary clearance is performed less frequently [27,28]. Our results are in line with those of past studies: pain, fatigue and sleeping disorders are important factors that need to be addressed throughout the breast cancer patients' care. Large studies, such as ours, are needed to investigate HRQoL in the pursuit to provide best possible treatment for each individual.

## Conclusions

Our study showed that reconstruction patients had good physical functioning and their sexual wellbeing was the least impaired of all study groups. Patients treated with oncoplastic resection had the best body image and their overall HRQoL reached a higher level already at 12 months after surgery whereas reconstruction patients needed a longer time to recover. Mastectomy patients had the lowest scores which needs to be taken into account when planning

**Table 3**

EORTC: Symptom, Functional and Breast cancer specific scores that differed statistically significantly between study groups at Baseline.<sup>B</sup> Bonferroni's test can't identify which groups differ, \*p < 0.05, \*\*p < 0.01, \*\*\*p < 0.001. Mean score, Standard Deviation and 95% Confidence Interval. Highest mean underlined.

Baseline	p	Resection			Oncoplastic Resection			Mastectomy			Reconstruction		
		Mean	SD	95% CI	Mean	SD	95% CI	Mean	SD	95% CI	Mean	SD	95% CI
<b>Pain</b>	0.038*	14.846	19.352	12.972; 16.720	12.014	15.782	10.007; 14.021	<u>17.391</u>	21.347	15.131; 19.652	10.544	12.589	6.928; 14.160
<b>Nausea</b>	0.001***	2.028	6.477	1.400; 2.656	1.250	6.527	0.420; 2.080	2.624	8.235	1.749; 3.499	<u>4.422</u>	8.856	1.878; 6.965
<b>Physical functioning</b>	0.001***	86.815	14.746	85.380; 88.250	89.177	12.875	87.537; 90.818	85.526	16.781	83.741; 87.311	<u>92.925</u>	11.419	89.645; 96.205
<b>Cognitive functioning</b>	0.003**	<u>92.233</u>	13.012	90.973; 93.493	91.144	14.313	89.320; 92.967	87.998	17.221	86.169; 89.827	90.476	14.434	86.330; 94.622
<b>Social functioning</b>	0.005**	91.361	16.505	89.757; 92.965	92.957	14.016	91.171; 94.743	88.462	20.301	86.289; 90.634	<u>95.833</u>	9.416	93.099; 98.567
<b>Body Image</b>	0.001***	<u>90.470</u>	14.928	88.997; 91.943	89.874	13.549	88.129; 91.619	84.003	21.739	81.670; 86.336	83.673	19.907	77.955; 89.391
<b>Sexual functioning</b>	0.045 <sup>B</sup>	27.792	26.728	25.093; 30.492	30.507	26.670	27.042; 33.972	26.614	27.354	23.581; 29.646	<u>36.111</u>	29.038	27.679; 44.543
<b>Future perspective</b>	0.003**	53.484	28.373	50.685; 56.284	<u>54.326</u>	25.486	51.051; 57.602	46.246	30.777	42.929; 49.564	51.020	28.949	42.705; 59.336
<b>Breast symptoms</b>	0.000***	10.762	13.564	9.439; 12.086	11.251	13.303	9.552; 12.950	<u>15.937</u>	16.795	14.143; 17.732	13.265	10.881	10.140; 16.391
<b>Arm symptoms</b>	0.027 <sup>B</sup>	8.703	13.163	7.419; 9.987	8.673	13.629	6.929; 10.417	<u>11.095</u>	16.321	9.351; 12.838	5.896	11.363	2.632; 9.160

**Table 4**

Means, Standard deviation and 95% Confidence intervals between groups regarding those EORTC Functional and Symptom scores that were statistically significantly different between groups at 24 Months.<sup>B</sup> Bonferroni's test can't identify which groups differ, \*p < 0.05, \*\*p < 0.01, \*\*\*p < 0.001. Highest mean underlined.

24 Months	p	Resection			Oncoplastic Resection			Mastectomy			Reconstruction		
		Mean	SD	95% CI	Mean	SD	95% CI	Mean	SD	95% CI	Mean	SD	95% CI
<b>Financial difficulties</b>	0.012*	7.123	20.022	5.062; 9.184	4.921	16.373	2.693; 7.148	<u>9.29</u>	19.988	7.037; 11.542	8.696	20.409	2.635; 14.756
<b>Physical functioning</b>	0.002**	82.511	17.506	80.714; 84.308	85.548	14.363	83.594; 87.502	81.832	17.654	79.836; 83.827	<u>90.519</u>	12.018	86.908; 94.129
<b>Body Image</b>	0.000***	85.808	19.623	83.794; 87.823	<u>86.019</u>	18.131	83.558; 88.48	70.500	27.367	67.391; 73.609	67.803	27.702	59.381; 76.225
<b>Sexual functioning</b>	0.046 <sup>B</sup>	26.6	26.079	23.854; 29.345	25.248	25.714	21.680; 28.815	22.569	25.803	19.577; 25.562	<u>32.576</u>	26.646	24.475; 40.677
<b>Arm symptoms</b>	0.000***	11.929	17.141	10.169; 13.688	15.377	18.368	12.884; 17.869	<u>19.616</u>	19.377	17.440; 21.792	10.386	13.334	6.427; 14.347

surgery for future patients. Wider use of oncoplastic techniques is associated with less mastectomies and probably higher HRQoL. Reconstructive surgery appears to, according to our results, provide good quality of life. In practice, for the planning of surgical options, these results could be useful: patients should be offered oncoplastic surgical treatment when applicable. Those, who require mastectomy, should be offered reconstructive options and they should be warned about the possibility that regaining good HRQoL may take a longer time.

### Author contributions

All authors participated in the designing and performing of this study and contributed to the writing of this article.

### Funding

The corresponding author received a personal grant from Kurt and Doris Palander Foundation for Medical Research for covering the writing process. The grant providers had no influence on the designing, performing or writing of this article.

### CRediT authorship contribution statement

**Mervi Rautalin:** Conceptualization, Methodology, Formal analysis, Investigation, Writing - original draft. **Tiina Jähkölä:** Conceptualization, Methodology, Writing - review & editing. **Risto P. Roine:** Conceptualization, Methodology, Data curation, Resources, Writing - review & editing, Supervision.

### Acknowledgements

Mr Timo Pessi, M. Sc., Elisa Oyj, Healthcare Solutions, Helsinki, Finland. Assisted and performed statistical analyses in collaboration with the corresponding author.

Breast Cancer Unit at Comprehensive Cancer Center in Helsinki University Hospital: we wish to thank the Unit for collaboration and all the breast cancer nurses who participated in the recruitment process with introducing the information letters and questionnaires to patients.

The corresponding author received a personal grant from Kurt and Doris Palander Foundation for Medical Research for covering the writing process. The grant providers had no influence on the designing, performing or writing of this article.

# Appendix. 115D Mean score by groups. \* MID $\geq 0.015$ change from baseline \*\* MID $\geq 0.015$ change from lowest measured timepoint within groups

15D mean score	Resection	Oncoplastic resection	Mastectomy	Reconstruction
Baseline	0.921	0.930	0.910	0.932
3 Months	0.895*	0.888*	0.881*	0.88*
6 Months	0.896	0.896	0.886	0.888
12 Months	0.898	0.906**	0.891	0.887
24 Months	0.897	0.904**	0.890	0.903**

## References

- Mansell J, Weiler-Mithoff E, Martin J, Khan A, Stallard S, Doughty JC, et al. How to compare the oncological safety of oncoplastic breast conservation surgery - to wide local excision or mastectomy? *Breast* 2015;24:497–501.
- Ojala K, Meretoja TJ, Leidenius MHK. Aesthetic and functional outcome after breast-conserving surgery - comparison between conventional and oncoplastic resection. *EJSO* 2017;43:658–64.
- Pukancsik D, Kelemen P, Ujhelyi M, Kovacs E, Udvarhelyi N, Meszaros N, et al. Objective decision making between conventional and oncoplastic breast-conserving surgery or mastectomy: an aesthetic and functional prospective cohort study. *EJSO* 2017;43:303–10.
- Pearce BCS, Fiddes RN, Paramanathan N, Chand N, Laws SAM, Rainsbury RM. Extreme oncoplastic conservation is a safe new alternative to mastectomy. *EJSO* 2019 Sep 5. <https://doi.org/10.1016/j.ejso.2019.09.004>. pii: S0748-7983(19)30664-X. [Epub ahead of print].
- Ej Campbell, L Romics. Oncological safety and cosmetic outcomes in oncoplastic breast conservation surgery, a review of the best level of evidence literature. *Breast Cancer* 2017;9:521–30. Published online 2017 Aug 4, 10.2147/BCTT.S113742 PMID: PMC5552002 PMID: 28831273.
- Howes BHL, Watson DI, Xu C, Fosh B, Canepa M, Dean NR. Quality of life following total mastectomy with and without reconstruction versus breast-conserving surgery for breast cancer: a case-controlled cohort study. *J Plast Reconstr Aesthetic Surg* 2016;69:1184–91.
- Jähkölä T. Self-perceptions of women after early breast cancer surgery. *EJSO* 1998;24:9–14.
- Sintonen H. The 15D instrument of health-related quality of life: properties and applications. *Ann Med* 2001;33(5):328–36. <https://doi.org/10.3109/07853890109002086>.
- The EORTC Quality of Life Group & EORTC Quality of Life Unit. Guidelines for assessing quality of life in EORTC Clinical Trials. Brussels: EORTC Data Center; 2002, ISBN 2-930064-27-7.
- Zehra S, Doyle F, Barry M, Walsh S, Kell MR. Health-related quality of life following breast reconstruction compared to total mastectomy and breast-conserving surgery among breast cancer survivors: a systematic review and meta-analysis. *Breast Cancer* 2020 Jul;27(4):534–66. <https://doi.org/10.1007/s12282-020-01076-1>. Epub 2020 Mar 12. PMID: 32162181.
- Stein MJ, Karir A, Arnaout A, Roberts A, Cordeiro E, Zhang T, et al. Quality-of-Life and surgical outcomes for breast cancer patients treated with therapeutic reduction mammoplasty versus mastectomy with immediate reconstruction. *Ann Surg Oncol* 2020;27:4502–12. <https://doi.org/10.1245/s10434-020-08574-8>.
- Rautalin M, Färkkilä N, Sintonen H, Saarto T, Taari K, Jähkölä T, et al. Health-related quality of life in different states of breast cancer - comparing different instruments. *Acta Oncol* 2018 May;57(5):622–8. <https://doi.org/10.1080/0284186X.2017.1400683>. Epub 2017 Nov 15. PMID: 29140139.
- Klein D, Mercier M, Abeilard E, Puyraveau M, Danzon A, Dalstein V, et al. Long-term quality of life after breast cancer: a French registry-based controlled study. *Breast Canc Res Treat* 2011 Aug;129(1):125–34. <https://doi.org/10.1007/s10549-011-1408-3>. Epub 2011 Feb 22. PMID: 21340477.
- Färkkilä N, Torvinen S, Roine RP, Sintonen H, Hänninen J, Taari K, et al. Health-related quality of life among breast, prostate, and colorectal cancer patients with end-stage disease. *Qual Life Res* 2014 May;23(4):1387–94. <https://doi.org/10.1007/s11136-013-0562-y>. Epub 2013 Nov 1. PMID: 24178630.
- Dauplat J, Kwiatkowski F, Rouanet P, Delay E, Clough K, Verhaeghe JL, et al. C. Pomel and the STIC-RMI working group: quality of life after mastectomy with or without immediate breast reconstruction. *BJS* 2017;104:1197–206.
- Kindts I, Laenen A, van der Akken M, Weltens C. PROMs following breast-conserving therapy for breast cancer: results from a prospective longitudinal monocentric study. *Support Care Canc* 2019;27:4123–32.
- Alanne S, Roine RP, Rasanen P, et al. Estimating the minimum important change in the 15D scores. *Qual Life Res* 2015;24:599–606.
- Osaba D, Rodrigues G, Pymes J, et al. Interpreting the significance of changes in health-related quality of life-scores. *J Clin Oncol* 1998;16:139–44.
- Cocks K, King MT, Velikova G, de Gastro Jr G, Martyn St-James M, Fayers PM, et al. Evidence-based guidelines for interpreting change scores for European organisation for the research and treatment of cancer quality of life questionnaire core 30. *Eur J Canc* 2012;48:1713–21.
- Clough KB, Kaufman GJ, Nos C, Buccimazza I, Im Sarfati. Improving breast cancer surgery: a classification and quadrant per quadrant atlas for oncoplastic surgery. *Ann Surg Oncol* 2010;17:1375–91.
- Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chron Dis* 1987;40(5):373–83.
- Quan H, Sundararajan V, Halfon P, Fong A, Burnand B, Luthi J-C, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. *Med Care* 2005;43:1130–9. 11.
- Quan H, Li B, Couris CM, Fushimi K, Graham P, Hider P, et al. Updating and validating the Charlson comorbidity index and score for risk adjustment in hospital discharge abstracts using data from 6 countries. *Am J Epidemiol* 2011;173:676–82. <https://doi.org/10.1093/aje/kwq433>. Epub 2011 Feb 17, 6.
- Theocharidis V, Katsaros I, Sgouroumellis E, Serifis N, Boikou V, Tasigiorgos S, et al. Current evidence on the role of smoking in plastic surgery elective procedures: a systematic review and meta-analysis. *J Plast Reconstr Aesthetic Surg* 2018;71:624–36.
- Boczar D, Huayllani MT, Forte AJ, Rinker B. Microsurgical breast reconstruction in the obese patient using abdominal flaps. *Ann Plast Surg* 2020. <https://doi.org/10.1097/SAP.0000000000002284>. 00:00-00.
- A. Toija, T. Kettunen, M. Leidenius, T. Vainiola, R.P. Roine. Effectiveness of peer support on health-related quality of life in recently diagnosed breast cancer patients: a randomized controlled trial. *Support Care Canc* <https://doi.org/10.1007/s00520-018-4499-0>.
- Donker M, van Tienhoven G, Straver ME, Meijnen P, van de Velde CJH, Mansel RE, et al. Radiotherapy or surgery of the axilla after a positive sentinel node in breast cancer (EORTC 10981-22023 AMAROS): a randomised, multi-centre, open-label, phase 3 non-inferiority trial. *Lancet Oncol* 2014;15:1303–10. 12.
- Moossdorff M, Nakhliis F, Hu J, Barry WT, Losk K, Haskett C, et al. The potential impact of AMAROS on the management of the axilla in patients with clinical T1-N0 breast cancer undergoing primary total mastectomy. *Ann Surg Oncol* 2018;25:2612–9.